

**REMARKS**

Claims 124-127 and 133-181 are pending in this application. Claims 124-127 and 133-181 are subject to restriction requirement.

Applicants respectfully traverse the restriction. However, in the event the Examiner rejects the below arguments, applicants hereby elect Group XVII (claims 174-176) for further prosecution, with traverse.

In the Office Action of November 1, 2006, the Examiner issued a second restriction requirement for claims 124-127 and 133-181 under 35 U.S.C. § 121. More specifically, the Examiner required restriction to one of twenty-three (23) groups, as described below:

- I. Claims 124-125, drawn to a method of synthesizing a bispecific antibody comprising VH antibody 1-S-VL antibody 1-S-VL antibody 2-S-VH antibody 2, classified in class 530, subclass 387.3.
- II. Claims 124-125, 133, drawn to a method of synthesizing a bispecific antibody comprising VH antibody 1-S-VL antibody 1-S-VH antibody 2-S-VL antibody 2, classified in class 530, subclass 387.3
- III. Claims 124-125, 133, drawn to a method of synthesizing a bispecific antibody comprising VL antibody 1-S-VH antibody 1-S-VL antibody 2-S-VH antibody 2, classified in class 530, subclass 387.3.
- IV. Claims 124-125, drawn to a method of synthesizing a bispecific antibody comprising VL antibody 1-S-VH antibody 1-S-VH antibody 2-S-VL antibody 2, classified in class 530, subclass 387.3.
- V. Claims 126, 134-135, drawn to a method of making a bispecific antibody comprising expressing the sequence VL antibody 1-S-VH antibody 2 and the sequence VH antibody 1-S-VL antibody 2 and combining the two products, classified in class 530, subclass 387.3
- VI. Claims 127, 136-137, drawn to a method of making a bispecific antibody comprising expressing the sequence VL antibody 2-S-VH antibody 1 and the sequence VH antibody 2-S-VL antibody 1 and combining the two products, classified in class 435, subclass 188.5 and class 530, subclass 387.3.

- VII. Claims 138-140, drawn to a method of making a bispecific antibody comprising expressing a single chain protein comprising the VH and VL regions of a first antibody and the VH and VL regions of a second antibody, classified in class 530, subclass 387.3.
- VIII. Claims 141-143, drawn to a method of making a bispecific antibody comprising expressing a single chain protein comprising the VH and VL regions of a first antibody and the VH and VL regions of a second antibody, expressing a single chain protein comprising the VL region of the first antibody and the VH regions of the second antibody and combining the two, classified in class 435, subclass 188.5 and class 530, subclass 387.3.
- IX. Claims 144-145, drawn to a method of making a bispecific antibody comprising expressing two single chain polypeptides, each comprising a VH and VL region, and combining the two single chain polypeptides, classified in class 530, subclass 387.3.
- X. Claims 176-177, drawn to an antibody comprising an antibody VH region from a first antibody and one antibody VL region from a second antibody, having the sequence VL antibody 2-S-VH antibody 1, classified in class 530, subclass 387.3.
- XI. Claims 176-177, drawn to an antibody comprising one antibody VH region from a first antibody and one antibody VL region from a second antibody, having the sequence VH antibody 1-S-VL antibody 2, classified in class 530, subclass 387.3.
- XII. Claims 146-159, 176, drawn to an antibody comprising one antibody VH region from a first antibody, one antibody VL region from a second antibody and further comprising a second VL region from the first antibody and a second VH region from the second antibody, having the sequence VH antibody 1-S-VL antibody 1-S-VL antibody 2-S-VH antibody 2, classified in class 435, subclass 188.5 and class 530, subclass 387.3.
- XIII. Claims 146-159, 176, drawn to an antibody comprising one antibody VH region from a first antibody, one antibody VL region from a second antibody and further comprising a second VL region from the first antibody and a second VH region from the second antibody, having the sequence VH antibody 1-S-VL antibody 1-S-VH antibody 2-S-VL antibody 2, classified in class 435, subclass 188.5 and class 530, subclass 387.3.
- XIV. Claims 146-159, 176, drawn to a n antibody comprising one antibody VH region from a first antibody, one antibody VL region from a second antibody and further comprising a second VL region from the first

antibody and a second VH region from the second antibody, having the sequence VL antibody 1-S-VH antibody 1-S-VL antibody 2-S-VH antibody 2, classified in class 435, subclass 188.5 and class 530, subclass 387.3.

- XV. Claims 146-159, 176, drawn to an antibody comprising one antibody VH region from a first antibody, one antibody VL region from a second antibody and further comprising a second VL region from the first antibody and a second VH region from the second antibody, having the sequence VL antibody 1-S-VH antibody 1-S-VH antibody 2-S-VL antibody 2, classified in class 435, subclass 188.5 and class 530, subclass 387.3.
- XVI. Claims 160-173, 176, drawn to an antibody comprising one antibody VH region from a first antibody, one antibody VL region from a second antibody and further comprising a second VL region from the first antibody and a second VH region from the second antibody, the sequence of the first polypeptide comprising VL antibody 1-S-VH antibody 2 and the second polypeptide comprising VH antibody 1-S-VL antibody 2, a vector containing the nucleic acid encoding the antibody, a host cell that produce the antibody, a bacteriophage containing the nucleic acid, classified in class 435, subclass 188.5, 320.1, 235.1, 252.3 and class 530, subclass 387.3.
- XVII. Claims 174-176, drawn to an antibody comprising an antibody VH region from a first antibody, one antibody VL region from a second antibody and further comprising a second single chain polypeptide comprising a VH region and a VL region, classified in class 530, subclass 387.3.
- XVIII. Claims 178-179, drawn to a gene encoding a polypeptide chain comprising the VH and VL from both a first antibody and a second antibody, the sequence being VH antibody 1-S-VL antibody 1-S-VL antibody 2-S-VH antibody 2, classified in class 536, subclass 23.4.
- XIX. Claims 178-179, drawn to a gene encoding a polypeptide chain comprising the VH and VL from both a first antibody and a second antibody, the sequence being VH antibody 1-S-VL antibody 1-S-VH antibody 2-S-VL antibody 2, classified in class 536, subclass 23.4.
- XX. Claims 178-179, drawn to a gene encoding a polypeptide chain comprising the VH and VL from both a first antibody and a second antibody, the sequence being VL antibody 1-S-VH antibody 1-S-VL antibody 2-S-VH antibody 2, classified in class 536, subclass 23.4.
- XXI. Claims 178-179, drawn to a gene encoding a polypeptide chain comprising the VH and VL from both a first antibody and a second

antibody the sequence being VL antibody 1-S-VH antibody 1-S-VL antibody 2-S-VL antibody 2, classified in class 536, subclass 23.4.

XXII. Claims 180-181, drawn to a gene encoding a polypeptide chain comprising one antibody VH region from a first antibody and a VL region from a second antibody, having the sequence VL antibody 2-S-VH antibody 1, classified in class 536, subclass 23.4.

XXIII. Claims 180-181, drawn to a gene encoding a polypeptide chain comprising one antibody VH region from a first antibody and a VL region from a second antibody, having the sequence VH antibody 1-S-VL antibody 2, classified in class 536, subclass 23.4

In the Office Action, the Examiner found the 23 groups as being independent or distinct from each other in that each of the groups is allegedly drawn to methods or bispecific antibodies having different combinations of antibody fragments. Therefore the Examiner found them as being structurally different and patentably distinct.

Applicants note that in the Office Action the groups have been mistakenly misnumbered. As such, although the total number of groups is listed as 16, the number of groups is actually 23.

In the previous Office Action, the Examiner issued a six-way restriction requirement which was traversed by Applicants. The present Office Action, without addressing any of Applicants arguments, inexplicably further divided the claims into a total of 23 groups. Applicants assert that this 23-way restriction requirement is improper and unreasonable.

By way of example, the claims include generic claim 176 directed to a recombinant antibody. The claims also include a number of claims that are dependent upon claims 176 and cover species that fall within the scope of the generic claim (*e.g.*, claims 146-156, 160-164, 168-170, 174-175 and 177). The Office Action further restricted these claims into 8 different groups by species. The Office Action required claim restriction and restriction of other

claims with nothing, but a declaratory statement that “inventions are distinct (*e.g.*, Office Action p. 6). Such declaratory statement falls far short of satisfying the Examiner’s burden:

The MPEP clearly states:

For purposes of initial requirement, a serious burden on the Examiner may be *prima facie* shown if the Examiner shows by appropriate explanation of separate classification, or separate status in the art, or a different field of search as defined in MPEP § 808.2.

[MPEP 803]

In fact, Applicants respectfully assert that the Examiner cannot meet any of these requirements. The groups directed at recombinant antibodies all have the same status in the art as demonstrated by their identical classifications. Furthermore, the close relationship between the groups (which differs primarily in the arrangement of antibody subcomponents) ensures: a) that they will be covered by a single field of search and b) that simultaneous examination of all the groups will, therefore, not place the burden on the Examiner.

While maintaining their objection to any restriction requirement for the reason stated above, Applicants also respectfully note that the Examiner may have confused the Restriction Requirement under 37 C.F.R. § 1.121 with the Election of Species Requirement under 37 C.F.R. § 1.141 which appears more appropriate under the circumstances.

Applicants also respectfully point out to the Examiner that all groups suggested by the Examiner belong to related classes and 18 out of 23 groups belong to the same class and even to the same subclass (*e.g.*, Groups I-XVIII belong to class 530, subclass 387.3). Additionally, contrary to the Examiner’s assertion, the antibodies of the claims are closely related, differing primarily in the arrangement of antibody subcomponents. Further, only one field of search is required due to the close relation between the different antibody structures and between the antibodies, the methods of making the antibodies and the genes, host cells, etc, that

code for or produce the antibodies. Finally, the Examiner provides no support for his restriction but for a one sentence declaratory statement. For all of these reasons, the restriction requirement is improper and should be withdrawn in its entirety.

**Rejection Under 35 U.S.C. § 112, ¶ 2**

Additionally, in the Office Action the Examiner found claim 161 confusing and indefinite for failure to provide antecedent basis for “first polypeptide” in line 2. Applicants have amended claim 176 herein to provide the antecedent basis for claim 161.

Likewise, the Examiner found claim 174 confusing and indefinite for failure to provide antecedent basis for “a second single chain polypeptide.” Applicants respectfully disagree with the Examiner in that no antecedent basis is required for a “second polypeptide chain” in line 2 of claim 174. Therefore, the withdrawal of the rejection of claims 161 and 174 under 35 U.S.C. § 112, ¶ 2 is respectfully requested.

Applicants respectfully request an interview with the Examiner to discuss the restriction requirement. It is Applicants’ understanding that Examiner Patterson has retired. Accordingly, Applicants respectfully request an opportunity to discuss the subject application with the newly appointed Examiner.

No extra fee is believed due except for the fee for a five-month extension of time.

However, the Director is hereby authorized to charge any required fees and credit any overpayments to Deposit Account No. 50-0540.

Respectfully submitted,

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By: Henry J Cittone/  
Henry J. Cittone, Reg. No. 57,206  
Barry Evans, Reg. No. 22,802  
Attorney for Applicants  
KRAMER LEVIN NAFTALIS & FRANKEL LLP  
1177 Avenue of the Americas  
New York, New York 10036  
(212) 715-9100 (phone)  
(212) 715-8000 (fax)